

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (currently amended) ~~A~~ A polypeptide comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild-type Fc region, such that said polypeptide binds an FcγR with an altered affinity relative to a polypeptide comprising a wild-type Fc region, provided that said at least one amino acid modification is not solely a substitution at any of positions 255, 258, 267, 269, 270, 276, 278, 280, 283, 285, 289, 292, 293, 294, 295, 296, 300, 303, 305, 307, 309, 322, 329, 332, 331, 337, 338, 340, 373, 376, 416, 419, 434, 435, 437, 438, 439 or does not have an alanine at any of positions 256, 290, 298, 312, 333, 334, 359, 360, 326, or 430; a lysine at position 330; a threonine at position 339; a methionine at position 320; a serine at position 326; an asparagine at position 326; an aspartic acid at position 326; a glutamic acid at position 326; a glutamine at position 334; a glutamic acid at position 334; a methionine at position 334; a histidine at position 334; a valine at position 334; or a leucine at position 334; a lysine at position 335 an asparagine at position 268; a glutamine at position 272; a glutamine, serine, or aspartic acid at position 286; a serine at position 290; a methionine, glutamine, glutamic acid, or arginine at position 320; a glutamic acid at position 322; a serine, glutamic acid, or aspartic acid at position 326; a lysine at position 330; a glutamine at position 335; or a methionine at position 301.
2. (previously presented) A polypeptide comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild-type Fc region, such that said polypeptide specifically binds FcγRIIIA with a greater affinity than a comparable polypeptide comprising the wild-type Fc region binds FcγRIIIA, provided that said at least one amino acid modification is not solely a substitution at positions 329, 331, or 332, or does not have an alanine at any of positions 256, 290, 298, 312, 326, 333, 334, 359, 360, or 430; a lysine at position 330; a threonine at position 339; a methionine at position 320; a serine at position 326; an asparagine at position 326; an aspartic acid at position 326; a glutamic acid at position 326; a glutamine at position 334; a glutamic acid at position 334; a methionine at

position 334; a histidine at position 334; a valine at position 334; a lysine at position 330; a lysine at position 335; or a leucine at position 334.

3. (previously presented) The polypeptide of claim 2, wherein said at least one amino acid modification comprises a set of substitutions selected from the group consisting of substitution at position 339 with valine and at position 347 with histidine; a substitution at position 251 with proline and at position 415 with isoleucine; a substitution at position 185 with methionine, and at position 218 with asparagine, and at position 292 with leucine, and at position 399 with glutamic acid; a substitution at position 290 with proline and at position 142 with proline; a substitution at position 141 with valine, at position 268 with leucine, at position 288 with glutamic acid, and at position 291 with serine; a substitution at position 133 with methionine, at position 149 with tyrosine, at position 205 with glutamic acid, at position 334 with asparagine, and at position 384 with lysine; a substitution at position 125 with leucine, at position 215 with isoleucine, and at position 408 with isoleucine; a substitution at position 395 with isoleucine; a substitution at position of 247 with histidine; a substitution at position 396 with histidine; a substitution at position 392 with arginine; a substitution at position 415 with isoleucine and at position 251 with phenylalanine; a substitution at position 301 with cysteine, at position 252 with leucine, and at position 192 with threonine; a substitution at position 315 with isoleucine; a substitution at position 132 with isoleucine; a substitution at position 162 with valine; a substitution at position 348 with methionine, at position 334 with asparagine, at position 275 with isoleucine, at position 202 with methionine, and at position 147 with threonine; a substitution at position 310 with tyrosine, at position 289 with alanine, and at position 337 with glutamic acid; a substitution at position 119 with phenylalanine, at position 371 with serine, at position 407 with valine, and at position 258 with aspartic acid; a substitution at position 409 with arginine and at position 166 with asparagine; a substitution at position 408 with isoleucine, at position 215 with isoleucine, and at position 125 with isoleucine; a substitution at position 396 with leucine; a substitution at position 385 with glutamic acid and at position 247 with histidine; a substitution at position 379 with methionine; a substitution at position 219 with tyrosine; a substitution at position 282 with methionine; a substitution at position 276 with isoleucine, at position 334 with asparagine, and at position 348 with methionine; a substitution at position 401 with valine; a substitution at position 280 with leucine and

at position 395 with serine; a substitution at position 222 with asparagine; a substitution at position 246 with threonine and at position 319 with phenylalanine; a substitution at position 243 with isoleucine and at position 379 with leucine; a substitution at position 246 with threonine and at position 396 with histidine; a substitution at position 268 with aspartic acid and at position 318 with aspartic acid; a substitution at position 288 with asparagine, at position 330 with serine, and at position 396 with leucine; a substitution at position 243 with leucine, at position 255 with leucine, and at position 318 with lysine; a substitution at position 334 with glutamic acid, at position 359 with asparagine, and at position 366 with serine; a substitution at position 377 with phenylalanine; a substitution at position 334 with isoleucine; a substitution at position 244 with histidine, at position 358 with methionine, at position 379 with methionine, at position 384 with lysine, and at position 378 with methionine; a substitution at position 247 with leucine; a substitution at position 217 with serine, at position 378 with valine, and at position 408 with arginine; a substitution at position 247 with leucine, at position 253 with asparagine, and at position 334 with asparagine; a substitution at position 288 with methionine and at position 334 with glutamic acid; a substitution at position 334 with glutamic acid and at position 380 with aspartic acid; a substitution at position 256 with serine, at position 305 with isoleucine, at position 334 with glutamic acid, and at position 390 with serine; a substitution at position 372 with tyrosine; a substitution at position 246 with isoleucine and at position 334 with asparagine; a substitution at position 335 with asparagine, at position 370 with glutamic acid, at position 378 with glutamic acid, at position 394 with methionine, and at position 424 with leucine; a substitution at position 320 with glutamic acid and at position 326 with glutamic acid; a substitution at position 224 with leucine; a substitution at position 375 with cysteine and at position 396 with leucine; a substitution at position 233 with aspartic acid and at position 334 with glutamic acid; and a substitution at position 334 with glutamic acid, at position 359 with asparagine, at position 366 with serine, and at position 386 with arginine.

4. (previously presented) A polypeptide comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild-type Fc region, such that said polypeptide specifically binds FcγRIIIA with a greater affinity than a comparable polypeptide comprising the wild-type Fc region binds

FcγRIIIA, and said polypeptide further specifically binds FcγRIIB with a lower affinity than a comparable polypeptide comprising the wild-type Fc region binds FcγRIIB, provided that said variant Fc region does not have an alanine at any of positions 256, 298, 333, or 334.

5. (previously presented) The polypeptide of claim 1 or 2, wherein said modification comprises at least one amino acid substitution in the Fc region.
6. (previously presented) The polypeptide of claim 1 or 2, wherein said amino acid modification comprises at least one amino acid modification in the CH2 domain of the Fc region.
7. (previously presented) The polypeptide of claim 6, wherein said amino acid modification comprises substitution of Pro 247 with another amino acid at that position.
8. (previously presented) The polypeptide of claim 1 or 2, wherein said amino acid modification comprises at least one amino acid modification in the CH3 domain of the Fc region.
9. (previously presented) The polypeptide of claim 8, wherein said amino acid modification comprises substitution at position 396 with another amino acid at that position.
10. (previously presented) The polypeptide of claim 1 or 2, wherein said amino acid modification comprises at least one amino acid modification in the CH2 domain and at least one amino acid modification in the CH3 domain of the Fc region.
11. (previously presented) The polypeptide of claim 6, wherein said amino acid modification in the CH2 domain comprises substitution at position 251, 292, 268, 288, 291, or 247 with another amino acid at that position.
12. (previously presented) The polypeptide of claim 8, wherein said amino acid modification in the CH3 domain comprises substitution at position 347, 415, 399, 383, 384, 407, 395, or 396 with another amino acid at that position.

13. (previously presented) The polypeptide of claim 10, further comprising at least one amino acid modification in the hinge region of the Fc region.
14. (previously presented) The polypeptide of claim 1 or 2, wherein said amino acid modification comprises at least one amino acid modification in the hinge region of the Fc region.
15. (previously presented) The polypeptide of any of claims 1, 2, or 4 wherein the Fc region of the parent polypeptide is a human IgG Fc region.
16. (previously presented) The polypeptide of claim 15, wherein the human IgG Fc region is a human IgG1, IgG2, IgG3, or IgG4 Fc region.
17. (previously presented) The polypeptide of claim 1 or 2 wherein said polypeptide is an antibody.
18. (previously presented) An antibody comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild-type Fc region, such that said antibody specifically binds Fc γ RIIIA with a greater affinity than a comparable antibody comprising the wild-type Fc region binds Fc γ RIIIA, and said antibody further specifically binds Fc γ RIIB with a lower affinity than a comparable antibody comprising the wild-type Fc region binds Fc γ RIIB, provided that said variant Fc region does not have an alanine at any of positions 256, 298, 333, or 334.
19. (previously presented) The antibody of claim 17, wherein said antibody is a monoclonal antibody, a humanized antibody, or a human antibody.
20. (canceled)
21. (canceled)
22. (canceled)
23. (canceled)
24. (canceled)

25. (currently amended) The antibody of ~~claims claim~~ claim 17 or 18, wherein said antibody specifically binds FcγRIIIA with at least two times greater affinity than a comparable antibody comprising the wild-type Fc region binds FcγRIIIA.
26. (previously presented) A therapeutic antibody that specifically binds a cancer antigen, said therapeutic antibody comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild-type Fc region, such that said therapeutic antibody specifically binds FcγRIIIA with a greater affinity than the therapeutic antibody comprising the wild-type Fc region binds FcγRIIIA, provided that said at least one amino acid modification is not solely a substitution at positions 329, 331, or 332, or does not have an alanine at any of positions 256, 290, 298, 312, 333, 334, 359, 360, or 430; a lysine at position 330; a threonine at position 339; a methionine at position 320; a serine at position 326; an asparagine at position 326; an aspartic acid at position 326; a glutamic acid at position 326; a glutamine at position 334; a glutamic acid at position 334; a methionine at position 334; a histidine at position 334; a valine at position 334; or a leucine at position 334.
27. (previously presented) A therapeutic antibody that specifically binds a cancer antigen, said therapeutic antibody comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild-type Fc region, such that said therapeutic antibody specifically binds FcγRIIIA with a greater affinity than a therapeutic antibody comprising the wild-type Fc region binds FcγRIIIA, and said therapeutic antibody further specifically binds FcγRIIB with a lower affinity than a therapeutic antibody comprising the wild-type Fc region binds FcγRIIB, provided that said variant Fc region does not solely have an alanine at any of positions 256, 298, 333, or 334.
28. (previously presented) The therapeutic antibody of claim 26 or 27, wherein said therapeutic antibody mediates antibody dependent cell mediated cytotoxicity 2-fold more effectively, than the therapeutic antibody comprising a wild-type Fc region.
29. (previously presented) The therapeutic antibody of claim 26 or 27, wherein said therapeutic antibody is Herceptin®, Rituxan®, IC14, PANOREX™, IMC-225, VITAXIN™, Campath 1H/LDP-03, LYMPHOCIDE™, or ZEVLIN™.

30. (previously presented) The therapeutic antibody of claim 26 or 27, wherein said cancer antigen is MAGE-1, MAGE-3, BAGE, GAGE-1, GAGE-2, N-acetylglucosaminyltransferase, p15, beta-catenin, MUM-1, CDK4, HER-2/neu, human papillomavirus-E6, human papillomavirus-E7, or MUC-1.
31. (previously presented) A method of treating cancer in a patient having a cancer characterized by a cancer antigen, said method comprising administering to said patient a therapeutically effective amount of a therapeutic antibody of claim 26 or 27.
32. (previously presented) The method of claim 31, wherein said cancer antigen is MAGE-1, MAGE-3, BAGE, GAGE-1, GAGE-2, N-acetylglucosaminyltransferase, p15, beta-catenin, MUM-1, CDK4, HER-2/neu, human papillomavirus-E6, human papillomavirus-E7, or MUC-1.
33. (previously presented) The method of claim 31, wherein said cancer antigen is a breast, ovarian, prostate, cervical, or pancreatic carcinoma antigen.
34. (previously presented) The method of claim 31 further comprising the administration of one or more additional cancer therapies.
35. (previously presented) The method of claim 34, wherein said additional cancer therapy is selected from the group consisting of chemotherapy, immunotherapy, radiation therapy, hormonal therapy, or surgery.
36. (previously presented) The method of claim 31, wherein said patient is human.
37. (previously presented) A pharmaceutical composition comprising a therapeutically effective amount of one or more of the polypeptides of claims 1 or 2, and a pharmaceutically acceptable carrier.
38. (currently amended) A pharmaceutical composition comprising a therapeutically effective amount of one or more of the antibodies of ~~claims~~ claim 17 ~~or 18~~, and a pharmaceutically acceptable carrier.
39. (previously presented) A pharmaceutical composition comprising a therapeutically effective amount of one or more of the therapeutic antibodies of claims 26 or 27, and a pharmaceutically acceptable carrier.

40. (previously presented) The pharmaceutical composition of claims 26 or 27, further comprising one or more additional anti-cancer agents.
41. (previously presented) The pharmaceutical compositions of claim 40, wherein said anti-cancer agents is a chemotherapeutic agent, a radiation therapeutic agent, a hormonal therapeutic agent, or an immunotherapeutic agent.
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55. (canceled)
56. (currently amended) A method of treating or managing cancer in a patient having a cancer characterized by a cancer antigen, said method comprising administering to said patient a therapeutically effective amount of one or more of the antibodies of ~~claims~~ claim 17, 18, 26 or 27.

57. (currently amended) A method of treating cancer in a patient having a cancer characterized by a cancer antigen, said method comprising administering to said patient a therapeutically effective amount of one or more of the antibodies of claim 17, 18, 26 or 27 that specifically bind said cancer antigen.
58. (previously presented) A method of treating an autoimmune disorder in a patient in need thereof, said method comprising administering to said patient a therapeutically effective amount of a molecule comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild type Fc region, such that said molecule specifically binds FcγRIIB with a greater affinity than a comparable molecule comprising the wild type Fc region, and said molecule further specifically binds FcγRIIA with a lower affinity than a comparable molecule comprising the wild type Fc region.
59. (previously presented) The method of claim 58, wherein said autoimmune disorder is rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, Rieter's Syndrome, psoriasis, or lupus erythematosus.
60. (previously presented) The method of claim 58 further comprising administering to said patient a therapeutically effective amount one or more anti-inflammatory agents.
61. (previously presented) The method of claim 58 further comprising administering to said patient a therapeutically effective amount one or more immunomodulatory agents.
62. (previously presented) The method of claim 61, wherein at least one immunomodulatory agent is a small organic molecule.
63. (previously presented) The method of claim 62, wherein the small organic molecule is methotrexate, leflunomide, cyclophosphamide, cyclosporin A, FK506, mycophenolate mofetil, rapamycin, mizoribine, deoxyspergualin, brequinar, malonitrolamide, steroid, or corticosteroid.
64. (previously presented) The method of claim 60, wherein at least one anti-inflammatory agents is a non-steroidal anti-inflammatory drug.

65. (previously presented) The method of claim 64, wherein the non-steroidal anti-inflammatory drug is aspirin, ibuprofen, diclofenac, nabumetone, naproxen, or ketoprofen.
66. (previously presented) A method of treating an infectious disease in a patient in need thereof, said method comprising administering to said patient a therapeutically effective amount of a molecule comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild type Fc region, such that said molecule specifically binds FcγRIIB with a greater affinity than a comparable molecule comprising the wild type Fc region, and said molecule further specifically binds FcγRIIA with a lower affinity than a comparable molecule comprising the wild type Fc region.
67. (previously presented) The polypeptide of claims 1 or 2, wherein said polypeptide specifically binds FcγRIIA with a 4-fold greater affinity than a comparable polypeptide comprising the wild type Fc region binds FcγRIIA.
68. (previously presented) The polypeptide of claims 1 or 2, wherein said polypeptide specifically binds FcγRIIA with an 8-fold greater affinity than a comparable polypeptide comprising the wild type Fc region binds FcγRIIA
69. (previously presented) The polypeptide of claims 1 or 2, wherein said polypeptide specifically binds FcγRIIA with a 10-fold greater affinity than a comparable polypeptide comprising the wild type Fc region binds FcγRIIA
70. (previously presented) The polypeptide of claims 1 or 2, wherein said polypeptide specifically binds FcγRIIA with a 100-fold greater affinity than a comparable polypeptide comprising the wild type Fc region binds FcγRIIA
71. (currently amended) The antibody of claim 17 ~~or 18~~, wherein said antibody specifically binds FcγRIIA with a 4-fold greater affinity than a comparable antibody comprising the wild type Fc region binds FcγRIIA.
72. (currently amended) The antibody of claim 17 ~~or 18~~, wherein said antibody specifically binds FcγRIIA with an 8-fold greater affinity than a comparable antibody comprising the wild type Fc binds FcγRIIA.

73. (currently amended) The antibody of claim 17 ~~or 18~~, wherein said antibody specifically binds FcγRIIIA with a 10-fold greater affinity than a comparable antibody comprising the wild type Fc binds FcγRIIIA.
74. (currently amended) The antibody of claim 17 ~~or 18~~, wherein said antibody specifically binds FcγRIIIA with a 100-fold greater affinity than a comparable antibody comprising the wild type Fc binds FcγRIIIA.
75. (previously presented) A polypeptide comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild-type Fc region, such that said polypeptide specifically binds FcγRIIIA with a greater affinity than a comparable polypeptide comprising the wild-type Fc region, and said polypeptide further specifically binds FcγRIIB with a lower affinity than a comparable polypeptide comprising the wild type Fc region binds FcγRIIB, wherein said at least one amino acid modification comprises a set of substitutions selected from the group consisting of a substitution at position 243 with isoleucine and at position 379 with leucine; a substitution at position 288 with asparagine, at position 330 with serine and at position 396 with leucine; a substitution at position 243 with leucine and at position 255 with leucine; a substitution at position 288 with methionine and at position 334 with glutamic acid; a substitution at position 316 with aspartic acid, at position 378 with valine, and at position 399 with glutamic acid; a substitution at position 315 with isoleucine, at position 379 with methionine, and at position 399 with glutamic acid; a substitution at position 243 with isoleucine, at position 379 with leucine, and at position 420 with valine; a substitution at position 392 with threonine and at position 396 with leucine; a substitution at position 293 with valine, at position 295 with glutamic acid, and at position 327 with threonine; a substitution at position 268 with asparagine and at position 396 with leucine; a substitution at position 319 with phenylalanine, at position 352 with leucine, and at position 396 with leucine; a substitution at position 248 with methionine; a substitution at position 247 with leucine and at position 420 with valine; a substitution 334 with glutamic acid and at position 292 with leucine.
76. (previously presented) The polypeptide of claim 75 wherein said polypeptide is an antibody.

77. (previously presented) The antibody of claim 76, wherein said antibody has an enhanced ADCC activity relative to a comparable antibody comprising the wild type Fc region.
78. (previously presented) A polypeptide comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification, wherein said at least one amino acid modification comprises substitution at position 255 with leucine and at position 396 with leucine.
79. (previously presented) A polypeptide comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification, wherein said at least one amino acid modification comprises substitution at position 370 with glutamic acid and at position 396 with leucine.
80. (previously presented) A polypeptide comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification, wherein said at least one amino acid modification comprises substitution at position 392 with threonine and at position 396 with leucine.
81. (previously presented) A polypeptide comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification, wherein said at least one amino acid modification comprises substitution at position 221 with glutamic acid, at position 270 with glutamic acid, at position 308 with alanine, at position 311 with histidine, at position 396 with leucine, and at position 402 with aspartic acid.
82. (previously presented) A polypeptide comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification, wherein said at least one amino acid modification comprises substitution at position 243 with leucine, at position 305 with isoleucine, at position 378 with aspartic acid, at position 404 with serine, and at position 396 with leucine.
83. (previously presented) A polypeptide comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification, wherein said at least one amino acid modification comprises substitution at position 284 with methionine, at position 298 with asparagine, at position 334 with glutamic acid, at position 355 with tryptophan, and at position 416 with threonine.

84. (new) The antibody of claim 18, wherein said antibody specifically binds FcγRIIIA with at least two times greater affinity than a comparable antibody comprising the wild-type Fc region binds FcγRIIIA.
85. (new) A pharmaceutical composition comprising a therapeutically effective amount of one or more of the antibodies of claim 18, and a pharmaceutically acceptable carrier.
86. (new) A method of treating or managing cancer in a patient having a cancer characterized by a cancer antigen, said method comprising administering to said patient a therapeutically effective amount of one or more of the antibodies of claim 17.
87. (new) A method of treating cancer in a patient having a cancer characterized by a cancer antigen, said method comprising administering to said patient a therapeutically effective amount of one or more of the antibodies of claim 17 that specifically bind said cancer antigen.
88. (new) The antibody of claim 18, wherein said antibody specifically binds FcγRIIIA with a 4-fold greater affinity than a comparable antibody comprising the wild type Fc region binds FcγRIIIA.
89. (new) The antibody of claim 18, wherein said antibody specifically binds FcγRIIIA with an 8-fold greater affinity than a comparable antibody comprising the wild type Fc binds FcγRIIIA.
90. (new) The antibody of claim 18, wherein said antibody specifically binds FcγRIIIA with a 10-fold greater affinity than a comparable antibody comprising the wild type Fc binds FcγRIIIA.
91. (new) The antibody of claim 18, wherein said antibody specifically binds FcγRIIIA with a 100-fold greater affinity than a comparable antibody comprising the wild type Fc binds FcγRIIIA.